Research Article

Assessment of Hupu Gum for its Mucoadhesive Property in the Design and Evaluation of Mucoadhesive Buccal Patches of Propranolol HCl

***Anu Pravallika Janipalli, Lohithasu Duppala, Chaitanya Krishna Mylangam, Janaki Devi Sirisolla, Venkata Ramana Murthy Kolapalli**

Division of Pharmaceutical Technology, Department of Pharmaceutical Sciences, Andhra University College of Pharmaceutical Sciences, Andhra Pradesh- 530003, India.

ABSTRACT

Objectives: There are no reports about assessment of the mucoadhesive property of formaldehyde treated hupu gum (HG). Hence the present study was undertaken to assessment of its mucoadhesive property of hupu gum in design of mucoadhesive buccal patches of Propanolol Hcl as a model drug. **Methods:** The prepared mucoadhesive buccal patches were compared with known muccoadhesive polymer, such as polyethylene oxide N 750. Poloxamer 407 is used as a penetration enhancer. The various physicomechanical parameters such as weight variation, folding endurance, thickness, surface pH, drug content, swelling studies and various *ex vivo* mucoadhesion parameters like mucoadhesive strength and force of adhesion were evaluated. *In vitro* diffusion studies as well as *ex vivo* drug release studies were performed. **Results and conclusion:** The results of the present investigation concluded that the formaldehyde treated hupu gum used as mucoadhesive polymer in development of buccal patches of propranolol Hcl were prepared by solvent casting method. Hupu gum is highly viscous, difficult to form buccal patches, due to this reason it is exposed to formaldehyde for 1hr to reduce its swelling nature. However, the variation in the release profile of propranolol Hcl due to different in the drug to polymer ratio. Finally, concluded that the formaldehyde treated hupu gum used as a mucoadhesive polymer.

Keywords: Formaldehyde treated hupu gum, in vitro diffusion studies, poloxamer 407, polyethylene oxide N 750 and propranolol Hcl

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***Address for correspondence:**
Anu Pravallika Janipalli,
Division of Pharmaceutical Technology, Department of Pharmaceutical Sciences, Andhra University College of Pharmaceutical Sciences, Andhra Pradesh- 530003, India.
E-mail: anu.janipalli@gmail.com

INTRODUCTION

In present days, researchers were focused on drug delivery system in a specific region of the body for enhancing bioavailability and to minimize the dose dependent side effects. Buccal drug delivery system provides a promising alternate to other conventional systemic drug administrative methods as well as buccal mucosa acts as an excellent site for the absorption of drugs due to its relatively permeable with rich blood supply [1, 2]. The buccal route of administration of drugs which facilitates that drug molecules were directly enter into the systemic circulation, to avoid the first-pass metabolism as well as drug degradation in the harsh gastrointestinal(GI) environment, which are associated with oral route of administration. The buccal route is safe, easily accessible for self-medication and easily accepted by patients. Buccal mucoadhesive patches can be easily administered and removed from site of application, also to stop the input of drug whenever desired. Buccal mucoadhesive patches provide flexibility than other drug delivery systems [3-6].

Hupu gum is having good swelling index and moderate viscosity with various applications such as additive in food industry, in the printing industry and adhesive in chemical industry. Hupugum, a natural polysaccharide was found to be safe and non toxic up to 5%. The earlier reports on hupu gum revealed that it is used as carrier in the design and evaluation of solid mixtures of rofecoxib for dissolution enhancement [7]. So, hupu gum was selected for its application in the design of mucoadhesive buccal patches of

propranolol HCl as model drug. Hupu gum (Kondagogu, Kolha or Silk-cotton) is the dried gummy exudate obtained from the deciduous tree of "*Cochlospermum religiosum* (L.) *Alston*" (synonym *Cochlospermum gossypium* (L) D.C.), belongs to family *Cochlospermaceae* (synonym *Bixaceae*). Hupu gum tree is abundantly found in hills and forests of Chittoor, East Godavari districts in Andhra Pradesh, Mayurbhanj district in Odisha, India [8]. Its applicability is reported for industries like paper, printing gum, nicotine sprays and in the preparations of lotions and pastes, it was not investigated for its applicability in the pharmaceutical field [9].

Propranolol HCl was taken as model drug. It is chemically 1-naphthalen-1-yloxy-3-(propan-2-ylamino) propan-2-ol and it is a synthetic, sympatholytic, non-selective beta-adrenergic receptor blocker with antianginal, antiarrhythmic (class II) and antihypertensive properties. It is competitively antagonizes beta-adrenergic receptors, thereby inhibiting beta-adrenergic reactions, such as vasodilation, and negative chronotropic and inotropic effects. It is soluble in alcohol, slightly soluble in chloroform, practically insoluble in ether. Propranolol HCl undergoes extensive and highly variable hepatic first-pass metabolism following oral route of administration [10-12]. In this present work an attempt to study the mucoadhesive property of formaldehyde exposed hupu gum on propranolol HCl taken as a model drug, finally compared with the known mucoadhesive polymers such as polyethylene oxide (PEO) N 750 and the prepared mucoadhesive buccal patches were evaluated. The buccal mucoadhesive patches were prepared by solvent casting method.

MATERIALS AND METHODS

Propranolol hydrochloride was obtained as gift sample from Dr. Reddy's Laboratories Ltd, Hyderabad, India. Hupu gum of Grade-I quality was purchased from M/s. Girijan Co-op Corporation Ltd., Visakhapatnam, India. Polyethylene oxide(PEO N 750) and poloxamer 407 were purchased from Sigma Aldrich, Steinheim, Germany. All the other chemicals were used of A.R grade, satisfying pharmacopoeial specifications.

Preparation of mucoadhesive buccal patches

Hupu gum is highly viscous and difficult to form patches. Hence it is exposed to formaldehyde for 1hr to reduce its swelling nature. To produce a unidirectional release, one side of the drug layer is coated with impermeable backing layer (cellulose acetate).600 mg of cellulose acetate was weighed and dissolved in 20 ml of acetone, to this 0.5 ml of glycerine was added as per the formula shown in (**Table 1**). The prepared solution was poured into a petriplate, kept at room temperature and allowed to dry. Thus, the backing layer was prepared. Required amounts of polymer, drug and penetration enhancer as per the formula shown in (**Table 1**) (priorly exposed hupu gum to formaldehyde and PEO) were dissolved in water separately. The solution containing drug and penetration enhancer (poloxamer 407) was added to the prepared polymer solution and stirred continuously using magnetic stirrer. The prepared solution was poured uniformly into a petriplate containing backing layer by solvent casting technique, and allowed to dry in oven at 40 ^{0}C.

Fourier transform infrared spectroscopy (FTIR)

FTIR spectra of hupu gum, pure propranolol Hcl, optimized hupu gum formulation (PHG10) and PEO N 750 formulations (PPEO7) compatibility were studied by KBr pellet method using FTIR spectrophotometer (M/s. Perkin–Elmer, 841, Spectrum one).The scanning range was 400-4000 cm-1 and resolution was 1 cm-1. To study any possible interaction between drug and the plant gum FTIR spectroscopic analysis were carried out. Infrared absorbance data was collected over the wave number ranged from 4000 cm-1 to 400 cm-1 and was expressed in cm-1

Mucoadhesive strength measurement

Detachment force was measured on a modified balance in which the right pan was removed. A plastic beaker was kept in left pan and both the sides were balanced by weights. The buccal mucosal tissue of porcine was collected from the local slaughter house and stored in normal saline solution.

Table 1: Formualtion chart of Propranolon Muccoahesive Buccal Patches

Formulation code*	Propranolol HCl (mg)	PEO N 750 (mg)	FE-HG (mg)	Poloxamer 407(mg)
PHG 1	283.5	-	999.3	-
PHG 2	283.5	-	1134	-
PHG 3	283.5	-	1417	-
PHG 4	283.5	-	999.3	40
PHG 5	283.5	-	1134	40
PHG 6	283.5	-	1134	80
PHG 7	283.5	-	1417	40
PHG 8	283.5	-	1417	80
PHG 9	283.5	-	1417	120
PHG 10	283.5	-	1417	160
PPEO 1	567	567	-	-
PPEO 2	567	1134	-	-
PPEO 3	567	1417.5	-	-
PPEO 4	567	1701	-	-
PPEO 5	567	1417.5	-	40
PPEO 6	567	1417.5	-	80
PPEO 7	567	1417.5	-	120
PPEO 8	567	1701	-	40
PPEO 9	567	1701	-	80
PPEO 10	567	1701	-	120
PPEO 11	567	1984.5	-	160
PPEO 12	567	2268	-	160

*All formulations contains Cellulose acetate-600 mg, Glycerine- 0.5 ml, Acetone- 20 ml.
FE-HG -Formaldehyde exposed Hupu gum, PEO N 750 -Polyethylene oxide N 750

The underlying connective tissue was separated and washed with pH 6.6 phosphate buffer. The mucosal membrane was carefully cut and attached to the glass slide with the mucosal side facing outwards using cyanoacrylate glue and this slide was attached to the petri plate and it was placed on the right side of the balance. The patch was attached to the glass slide facing the drug polymer layer outwards using cyanoacrylate glue. The glass slide was suspended on the right hand side using a non elastic thread and the height of thread was adjusted. The mucous layer and the patch were wetted with pH 6.6 phosphate buffer and the patch was fixed to the mucus layer by applying a little pressure with the thumb and kept undisturbed for 5 min. On left hand side, water was added slowly in to a plastic beaker with the help of a burette till the patch just separated from the membrane surface. The weight of water in grams required to detach the patch was noted. The results were shown in (**Table 2**).

Mucoadhesion strength was calculated in Newtons by using the formula:

Force of adhesion (N) = Mucoadhesive strength X 9.81 / 1000.

Determination of *ex vivo* residence time

The *ex vivo* residence time was determined using USP dissolution apparatus II. The buccal mucosa of porcine which was previously washed was attached to the glass slide with the mucosal side facing outwards using cyanoacrylate glue. This was horizantally fixed to paddle of the dissolution apparatus. Drug polymer layer of patch was wetted with 0.5 ml of pH 6.6 phosphate buffer and attached to the mucus tissue with a little pressure to develop initial contact. 900 ml of pH 6.6 phosphate buffer was used as medium maintained at 37°C at 20 rpm. The time necessary for complete erosion or detachment of the patch from the mucosal surface was recorded. The results were shown in (**Table 2**).

Weight variation and thickness

For evaluation of weight variation three patches (each of 1sqcm) of every formulation were taken and weighed individually on a digital balance. The average weights were calculated. Similarly, three patches (each of 1sqcm) of each formulation

were taken and the film thickness was measured using micrometer screw gauge at three different places and the mean value was calculated and shown in the (**Table 3**).

Surface pH study

To evaluate the surface pH, buccal patches were left to swell for 2hrs in the 6.6 phosphate buffer. The surface pH was measured by means of a pH paper (range of 2-14) placed on the surface of the swollen patch and pH was measured and values are shown in (**Table 3**).

Folding endurance

The folding endurance of patches was determined by folding a patch repeatedly at the same place till it broke or was folded up to 300 times without breaking. The number of times, the film could be folded at the same place without breaking was noted as folding endurance in the (**Table 3**).

Drug content

To estimate the drug content for hupu gum(5mg/sqcm) and PEO N 750 (10mg/sqcm), three patch units (each of 1sqcm) from each formulation were taken and dissolved in 20 ml of 6.6 phosphate buffer by continues stirring using magnetic stirrer. The solution was diluted suitably with the pH 6.6 phosphate buffer and analysed at 289 nm using UV spectrophotometer and results are shown in the (**Table 3**).

Swelling studies

2.5% agar gel was prepared and poured in to a petri dish and allowed to solidify. Buccoadhesive patches were weighed individually (W_1) and placed in petri dish with the drug polymer layer facing agar gel and allowed to swell. The patches were removed at time intervals of 1, 2, 3, 4, 5, 6, 7 and 8 hrs from the petri dish and excess surface water was removed carefully with the tissue paper. The swollen patches were then reweighed (W_2). This experiment was performed in triplicate. The swelling index was calculated according to the following equation and results are shown in the (**Fig. 2**).

Swelling index = $(W_2-W_1)/W_1 \times 100$

***In-vitro* diffusion studies**

The release studies were determined by Franz diffusion cell. The dialysis membrane pore size of 50mm acts as a permeability barrier and pH 6.6 phosphate buffer acts as a medium. The patch of desired size was placed on the dialysis membrane and kept between 2 compartments. The receptor compartment contains 30 ml of pH 6.6 phosphate buffer and hydrodynamics was maintained by stirring with a magnetic bead at 400-500 rpm. At regular intervals 2 ml of sample was withdrawn from the receptor compartment and replaced with 2 ml of fresh medium. The samples collected were diluted suitably and analysed at 289 nm using UV spectrophotometer and the results were shown in the (**Fig. 3**).

Release kinetics

The analysis of drug release mechanism from a pharmaceutical dosage form is an important but complicated process and is practically evident in the case of matrix systems. As a model dependent approach, the dissolution data was fitted to popular release models such as zero-order, first-order, Higuchi, erosion and peppas equations. The order of drug release from matrix systems was determined by using zero order kinetics or first order kinetics. The mechanism of drug release from matrix systems was studied by using Higuchi equation, erosion and peppas equation and the results were shown in the (**Table 4**).

***Ex-vivo* release studies**

Ex vivo buccal permeation of propranolol HCl was studied with fresh porcine buccal mucosa as a barrier membrane. The buccal pouch of freshly sacrificed animal was procured from local slaughter house and was used within 2 hrs. The buccal mucosa was excised and trimmed evenly from the sides underlying connective tissue was removed. The membrane was washed with mammalian ringer solution and then with phosphate buffer (pH 6.6). The *Ex vivo* permeation studies were carried out using the modified Franz diffusion cell at 37ºC ± 0.2ºC. A patch of (1sqcm) of optimised formulation under study was placed in intimate contact with the excised porcine buccal mucosa magnetic bead was placed in the receptor compartment filled with 30 ml of pH 6.6 phosphate buffer. The cell contents were stirred with a magnetic stirrer and temperature of 37 ºC ± 0.2 ºC was maintained throughout the experiment. The samples were withdrawn at predetermined time intervals, filtered, diluted suitably, and

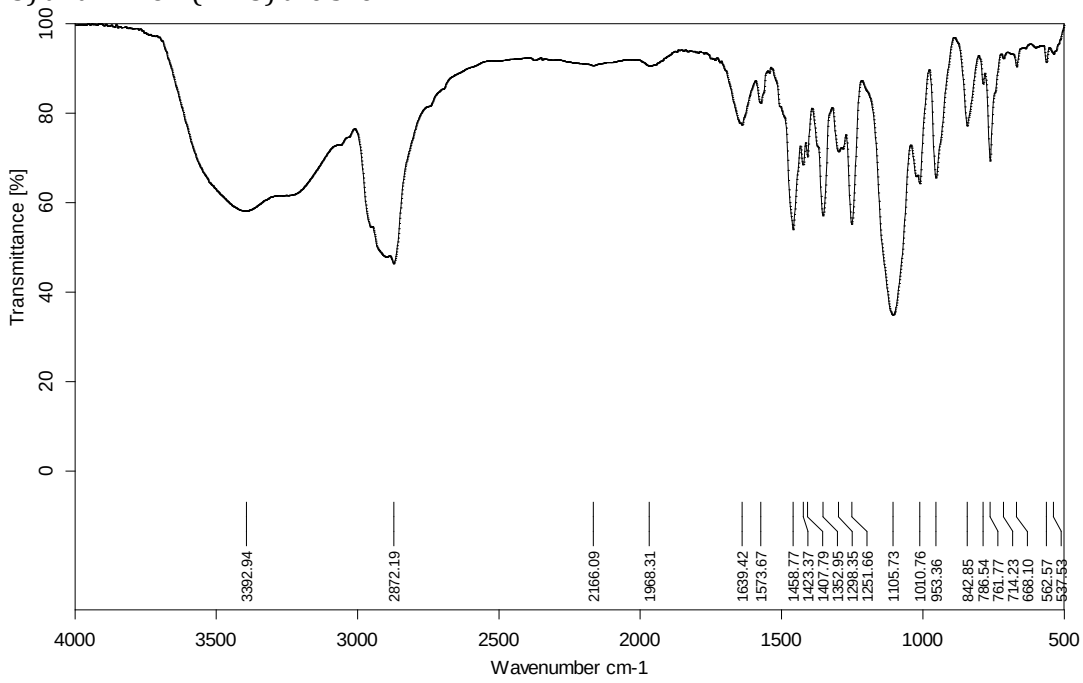
then analyzed using UV-spectrophotometer at 289 nm and the results were shown in (**Fig. 4**).

RESULTS AND DISCUSSION

Fourier transform infrared spectroscopy (ftir)

The FTIR spectra of pure drug propranolol HCl, pure polymers hupu gum, PEO N 750 and penetration enhancer poloxamer 407 and their respective selected formulations PHG10 (1:5) and PPEO7 (1:2.5) are shown in (**Fig. 1**). Presence of hupu gum and PEO N 750 and other excipients did not produce any major shift in principal peaks of propranolol HCl and also the presence of one ingredient did not produce shift in the peaks of other ingredients. This indicates that there is no interaction between drug and the excipients used in the study. Hence FTIR spectral analysis proved the compatibility of the drug and excipients used in the study.

a)



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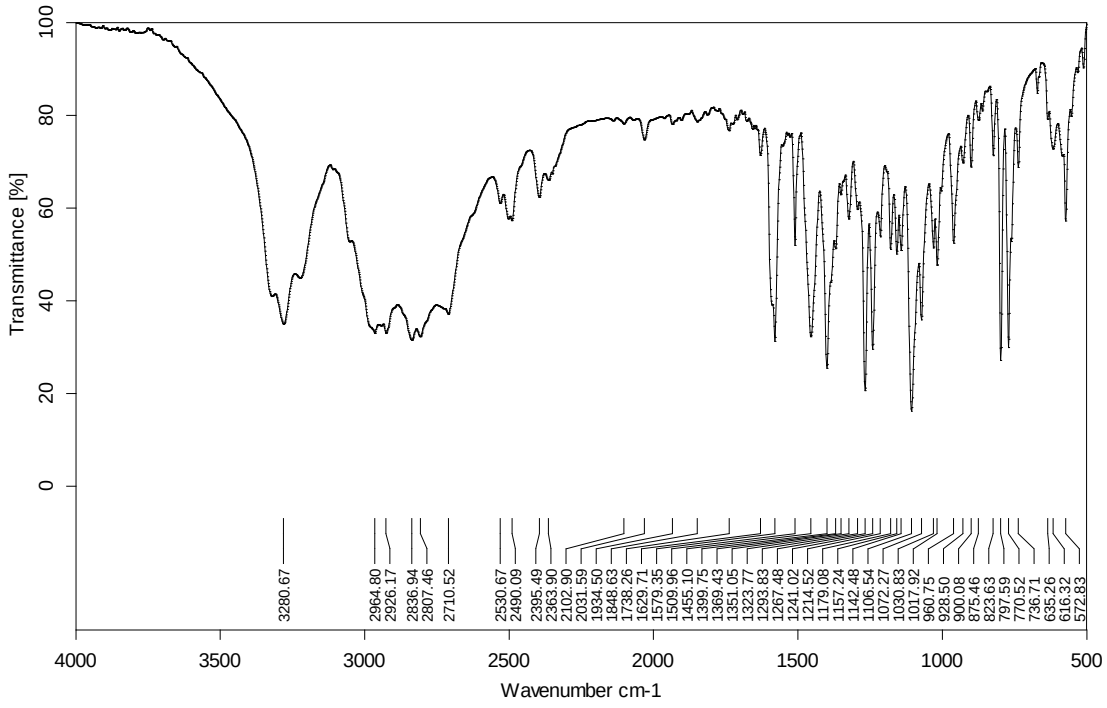


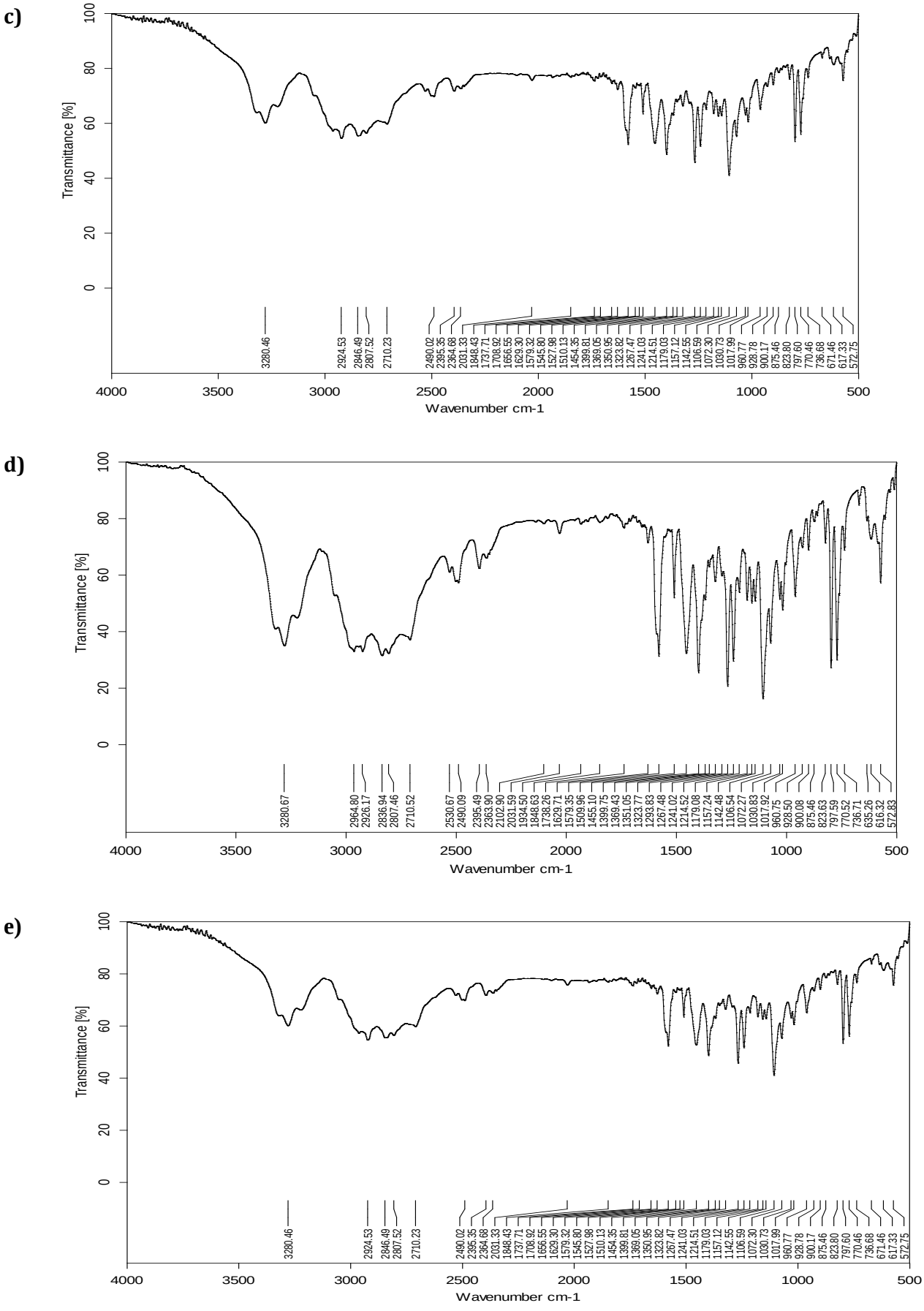


Figure 1: FTIR spectrum of a)Prapanolo Hcl; b) hupu gum; c)PEO N 750; d) Hupu gum formulation (PHG10); e) PEO N 750 formulations (PPEO7)

Mucoadhesive strength measurement

Mucoadhesive strength measurement was conducted for all formulations prepared with hupu gum and PEO N 750. Formulations containing hupu gum with different drug to polymer ratios are PHG1(1:3.5), PHG 4 (1:3.5), PHG 2(1:4), PHG 5(1:4), PHG 6 (1:4) and PHG 3(1:5), PHG7(1:5), PHG 8(1:5), PHG 9(1:5), PHG 10 (1:5) having 0.1%, 0.2%, 0.3%, 0.4% of penetration enhancer (poloxamer 407) respectively were shown in the (**Table 2**). While, those prepared with PEO N 750 are PPEO1 (1:1), PPEO2 (1:2), PPEO3(1:2.5), PPEO5(1:2.5), PPEO6(1:2.5), PPEO7 (1:2.5), PPEO4(1:3), PPEO8(1:3), PPEO9(1:3), PPEO10 (1:3), PPEO11 (1:3.5) and PPEO12 (1:4) with 0.1%, 0.2%, 0.3%, 0.4% of penetration enhancer respectively were shown in the (**Table 2**). The maximum mucoadhesion force (N) was observed for the formulations PHG10 (0.148) and PPEO12 (0.125) where as low mucoadhesion force (N) for the formulations PHG1 is 0.096 and PPEO1 is 0.067. Among the formulations prepared with hupu gum (PHG10) having mucoadhesive force (N) 0.148 and for PEO N750 (PPEO7) having mucoadhesive force (N) 0.096.

***Ex vivo* residence time**

Evaluation of *ex vivo* residence time was conducted for all formulations prepared with hupu gum and PEO N 750. Formulations containing hupu gum with different drug to polymer ratios are PHG1(1:3.5), PHG 4 (1:3.5), PHG 2(1:4), PHG 5(1:4), PHG 6 (1:4) and PHG3(1:5), PHG7 (1:5), PHG 8(1:5), PHG 9 (1:5), PHG10 (1:5) having 0.1%, 0.2%, 0.3%, 0.4% of penetration enhancer (poloxamer 407) respectively were shown in the (**Table 2**). While, those prepared with PEO N 750 are PPEO1 (1:1), PPEO2 (1:2), PPEO3 (1:2.5), PPEO5 (1:2.5), PPEO6 (1:2.5), PPEO7 (1:2.5), PPEO4(1:3), PPEO8(1:3), PPEO9(1:3), PPEO10 (1:3), PPEO11 (1:3.5) and PPEO12 (1:4) with 0.1%, 0.2%, 0.3%, 0.4% of penetration enhancer respectively were shown in the (**Table 2**). *Ex vivo* residence time varied from 6-8.5 hrs for the formulations prepared with hupu gum while those prepared with PEO N 750 varied from 1.5-4 hrs. It was found that as the concentration of polymer increased, the time of residence increased. Among the formulations prepared with hupu gum (PHG10) and PEO N 750 (PPEO7) showed 8.5 and 2.5 hrs respectively.

Table 2: *Ex vivo* residence time and mucoadhesive strength of propranolol HCl patches

Formulation Code	Mucoadhesive residence time (Mean ± s.d)(n=3)	Mucoadhesion Force (N) (mean ± s.d)(n=3)
PHG1	6 ± 0.56	0.096 ± 0.097
PHG2	7 ± 0.86	0.111 ± 0.098
PHG3	8 ± 0.63	0.132 ± 0.135
PHG4	6 ± 0.32	0.100 ± 0.072
PHG5	7 ± 0.65	0.117 ± 0.031
PHG6	7 ± 0.19	0.123 ± 0.179
PHG7	8 ± 0.49	0.134 ± 0.044
PHG8	8 ± 0.82	0.137 ± 0.017
PHG9	8 ± 0.16	0.143 ± 0.208
PHG10	8.5 ± 0.56	0.148 ± 0.069
PPEO1	1.5 ± 0.47	0.067 ± 0.137
PPEO2	2 ±0.23	0.075 ± 0.241
PPEO3	3 ± 0.85	0.084 ± 0.256
PPEO4	3.5 ± 0.95	0.095 ± 0.251
PPEO5	2 ± 0.32	0.086 ± 0.103
PPEO6	2.5 ± 0.65	0.09 ± 0.321
PPEO7	2.5 ± 0.83	0.096 ± 0.305
PPEO8	3 ± 0.88	0.100 ± 0.319
PPEO9	3.5 ± 0.56	0.105 ± 0.271
PPEO10	3.5 ± 0.63	0.107 ± 0.071
PPEO11	4 ± 0.65	0.114 ± 0.233
PPEO12	4 ± 0.56	0.125 ± 0.653

Weight variation and thickness

Weight of the patches was found to be in the range of 33.1 to 48 mg for hupu gum and PEO N750 in the range of 39.2 to 62.8 mg. As the proportion of the polymers is increasing, correspondingly the weight of the patches is increasing. The thickness of the buccal patch increases with increase in the amount of polymer. The maximum thickness was observed for the formulations PHG10 (0.586) and PPEO12 (0.556) where as minimum thickness was observed for the formulations PHG1 is and PPEO1 is 0.493 and 0.303.The average thickness of the cellulose acetate prepared backing layer was 0.3 mm. Among all the formulations prepared with hupu gum (PHG 10) showed thickness 0.586 mm and for PEO N750 (PPEO7) showed thickness 0.466 mm.

Surface pH study

The surface pH of prepared patches was measured with pH paper, values were found to be in the range of 6-7. This shows that the formulations were suitable for buccal drug delivery as pH was within the range of buccal cavity**.**

Folding endurance

All the patches did not show any deformation of patch after 300 times folding, which results that the all are having satisfactory flexibility.

Table 3: Characteristics of propranolol HCl patches

Formulation Code	Thickness (mean ± s.d) (n=3)	Weight variation (mean ± s.d) (n=3)	Surface p^H	Folding endurance	Drug content (mean ± s.d) (n=3)
PHG1	0.493 ± 0.003	33.10 ± 0.31	6-7	> 300	96.23 ± 0.23
PHG2	0.523 ± 0.003	40.23 ± 0.11	6-7	> 300	97.56 ± 0.56
PHG3	0.563 ± 0.003	44.20 ± 0.25	6-7	> 300	98.16 ± 0.12
PHG4	0.500 ± 0.003	34.21 ± 0.14	6-7	> 300	98.22 ± 0.52
PHG5	0.523 ± 0.003	40.41 ± 0.45	6-7	> 300	95.26 ± 0.15
PHG6	0.526 ± 0.003	40.80 ± 0.23	6-7	> 300	97.13 ± 0.23
PHG7	0.570 ± 0.003	44.40 ± 0.08	6-7	> 300	98.66 ± 0.15
PHG8	0.573 ± 0.003	45.00 ± 0.33	6-7	> 300	98.11 ± 0.12
PHG9	0.576 ± 0.003	47.50 ± 0.32	6-7	> 300	95.13 ± 0.45
PHG10	0.586 ± 0.003	48.00 ± 0.26	6-7	> 300	99.16 ± 0.16
PPEO1	0.303 ± 0.003	39.20 ± 0.31	6-7	> 300	96.63 ± 0.27
PPEO2	0.416 ± 0.003	39.40 ± 0.23	6-7	> 300	97.81 ± 0.11
PPEO3	0.446 ± 0.003	45.40 ± 0.11	6-7	> 300	96.72 ± 0.26
PPEO4	0.523 ± 0.003	50.80 ± 0.21	6-7	> 300	98.52 ± 0.11
PPEO5	0.456 ± 0.003	45.80 ± 0.33	6-7	> 300	95.53 ± 0.41
PPEO6	0.456 ± 0.003	46.00± 0.51	6-7	> 300	97.62 ± 0.50
PPEO7	0.466 ± 0.003	47.4 ± 0.63	6-7	> 300	99.45 ± 0.13
PPEO8	0.526 ± 0.003	51.00 ± 0.23	6-7	> 300	96.85 ± 0.12
PPEO9	0.536 ± 0.003	51.2 ± 0.22	6-7	> 300	99.76 ± 0.15
PPEO10	0.54 ± 0.003	52.6 ± 0.55	6-7	> 300	98.56 ± 0.15
PPEO11	0.546 ± 0.003	56.7 ± 0.12	6-7	> 300	96.53 ± 0.61
PPEO12	0.556 ± 0.003	62.8 ± 0.23	6-7	> 300	97.71 ± 0.18

Swelling studies

The patches prepared with hupu gum and PEO N750 has shown good swelling property and swelling index was increased with increase in the concentration for both the polymers. Formulations prepared with hupu gum has shown high swelling index than formulations prepared with PEO N750. Swelling index was measured for 8 hrs. The % swelling index is increased up to 5 hrs for PEO N750, but after that there was a decrease in the swelling of PEO N750 formulations where as hupu gum gradual swelling was observed.

***In-vitro* diffusion studies**

The *in vitro* diffusion studies of the formulated patches revealed that drug release from the patches depends on the concentration of polymer used in the formulation. In the present work, the formulations are designed to release the drug over a period of 6 hrs. Formulations

prepared with hupu gum were PHG 6 and PHG 10 released 94% and 99% of the drug in 6 hrs respectively are shown in the (**Fig. 3**). Formulations prepared with PEO N 750 were PPEO1 and PPEO7 released 100% and 99.5% of the drug in 3 hrs, and 6 hrs respectively are shown in the (**Fig. 3**). Based on the *in vitro* drug release studies and other the evaluated me formulations prepared with hupu gum and PEO N 750 PHG10 and PPEO7 were selected as the optimized formulations as these formulations showed 99% and 99.5% drug release for a desired period of 6 hrs which is suitable in the design of buccoadhesive patches of propranolol hydrochloride.

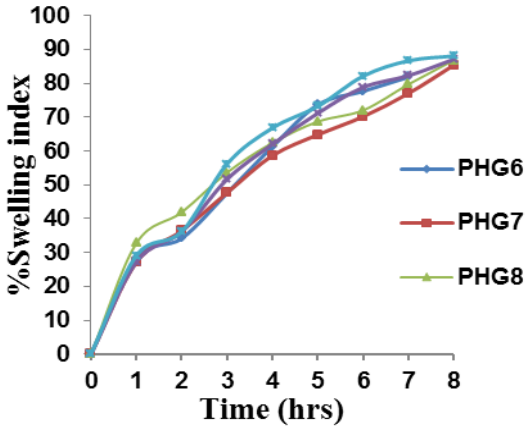
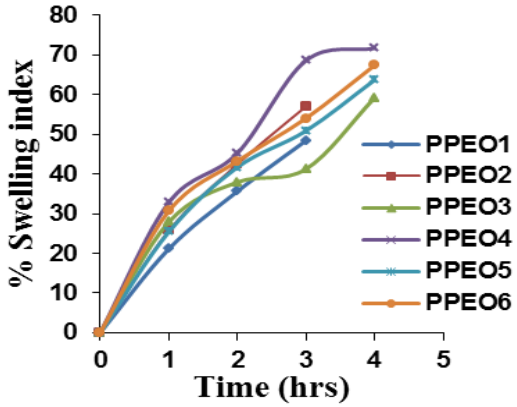
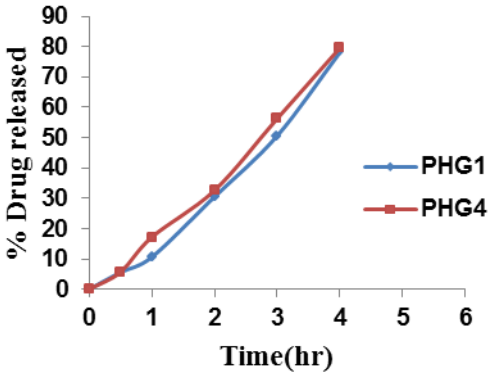
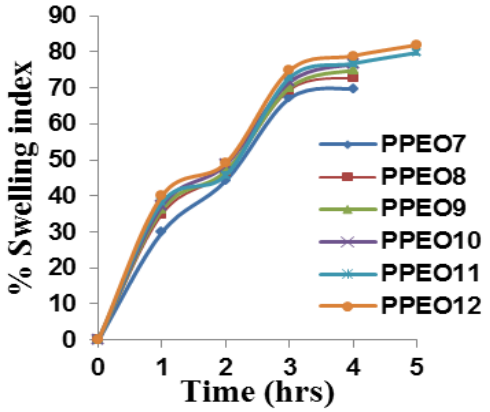
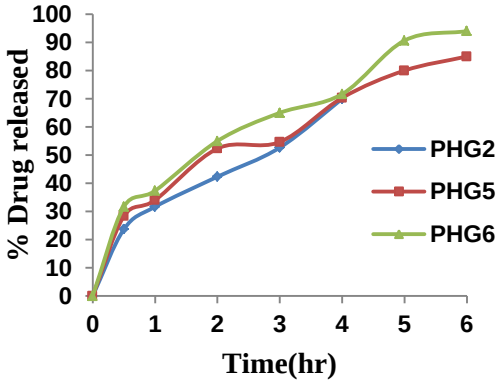


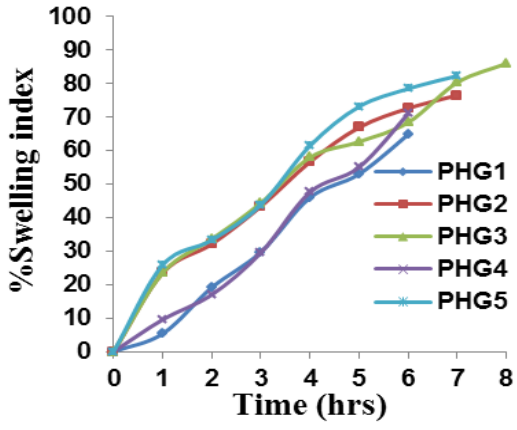
Figure 2: Swelling index studies of different formulations of propranolol HCl patches

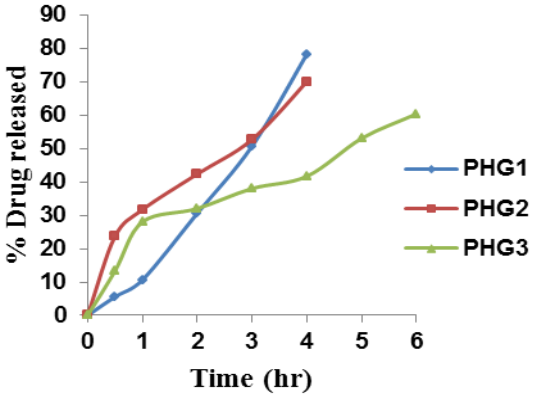


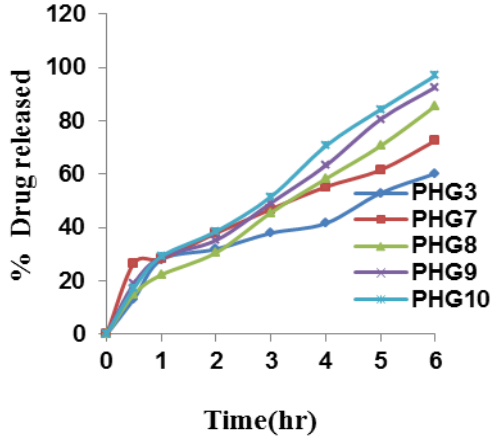


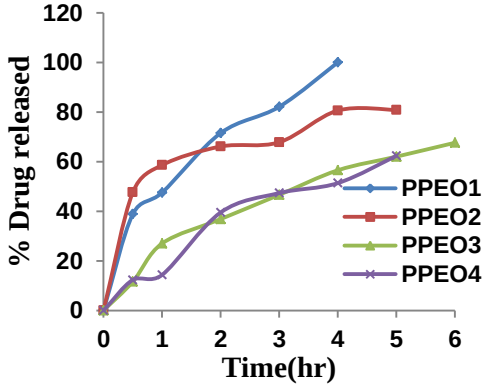


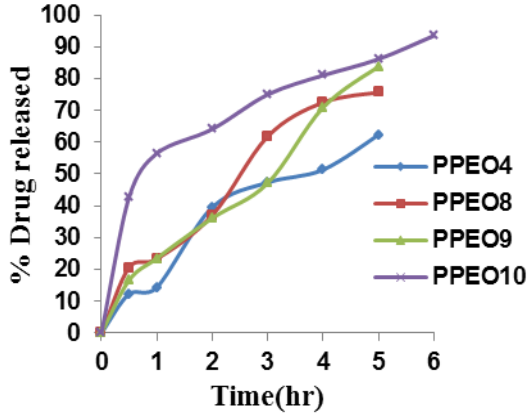


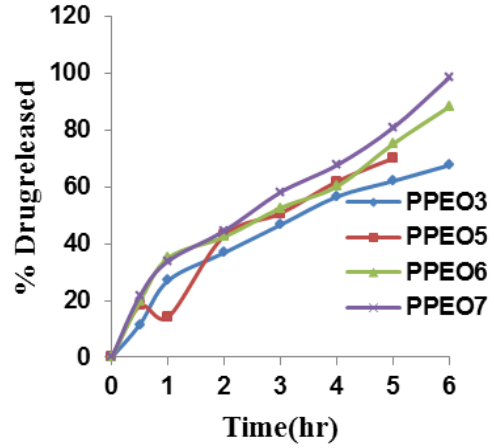












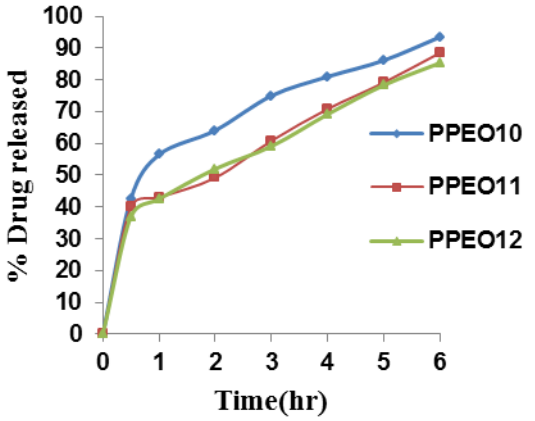


Figure 3: Diffusion profile of various mucoadhesive buccal patches of propranolol HCl

Release kinetics

In order to establish the mechanism of drug release, the data was fitted into popular exponential equations namely zero order, first order, Higuchi, Peppas and erosion and release kinetics of all formulations are shown in the (**Table 4**). The drug release kinetics from the hupu gum based formulation followed first-order kinetics (0.921-0.996) except the formulations PHG1, PHG9 and PHG10 which followed zero-order kinetics(0.946-0.992).The drug release kinetics from the PEO N750 based formulations also followed first order kinetics (0.918-0.992) except the formulations PPEO1, PPEO7 and PPEO9 which followed zero order kinetics(0.951-0.992). The relative contributions of drug diffusion and matrix erosion to drug release were further confirmed by subjecting the diffusion data to Higuchi and erosion models. It was found that all the formulations made with hupu gum and PEO N 750 followed diffusion mechanism (0.975-0.999) except the formulations PHG1, PHG4, PPEO4, PPEO5, and PPEO6 followed erosion mechanism (0.965-0.983) as indicated by their 'r' values. Also, the type of diffusion was non-Fickian diffusion as observed from the 'n' values of Peppas equation which were ranging from (0.458-0.884).

***Ex-vivo* release studies**

Ex vivo drug release studies were done for the optimized formulation of hupu gum (PHG10) and PEO N 750 (PPEO). PHG10 showed 90% drug release whereas PPEO7

showed 91.5% drug release. The release rate was decreased in *ex-vivo* studies when compared to *in vitro* studies.

Table 4: Correlation coefficient (r) values and release kinetics of propranolol HCl muccoadhesive buccal patches

Formulation code	Zero order		First order		Peppas		Higuchi	Erosion
	K_0	r	K_1	r	N	r	r	R
PHG1	19.53	0.946	0.356	0.99	0.458	0.999	0.912	0.965
PHG2	15.21	0.966	0.264	0.98	0.548	0.981	0.991	0.981
PHG3	19.53	0.958	0.133	0.977	0.548	0.959	0.986	0.973
PHG4	20.03	0.991	0.377	0.996	0.808	0.996	0.931	0.976
PHG5	12.57	0.955	0.294	0.989	0.508	0.987	0.994	0.986
PHG6	13.9	0.958	0.435	0.969	0.514	0.993	0.991	0.983
PHG7	10.11	0.958	0.294	0.983	0.514	0.995	0.991	0.980
PHG8	13.34	0.991	0.435	0.995	0.764	0.988	0.983	0.973
PHG9	14.26	0.990	0.377	0.945	0.673	0.973	0.975	0.975
PHG10	15.28	0.992	0.488	0.921	0.693	0.984	0.979	0.971
PPEO1	22.01	0.951	0.985	0.918	0.521	0.995	0.995	0.941
PPEO2	12.2	0.817	0.287	0.929	0.499	0.985	0.985	0.898
PPEO3	10.48	0.967	0.188	0.992	0.525	0.997	0.997	0.987
PPEO4	12.21	0.971	0.188	0.986	0.870	0.957	0.957	0.983
PPEO5	13.75	0.973	0.237	0.991	0.866	0.962	0.962	0.988
PPEO6	12.48	0.975	0.732	0.976	0.508	0.970	0.970	0.979
PPEO7	14.49	0.983	0.534	0.866	0.581	0.986	0.986	0.943
PPEO8	15.16	0.975	0.294	0.987	0.852	0.986	0.986	0.984
PPEO9	15.88	0.992	0.336	0.965	0.884	0.986	0.986	0.981
PPEO10	12.13	0.880	0.384	0.979	0.775	0.991	0.991	0.966
PPEO11	11.78	0.926	0.303	0.974	0.528	0.999	0.999	0.973
PPEO12	11.49	0.925	0.276	0.982	0.662	0.992	0.992	0.974

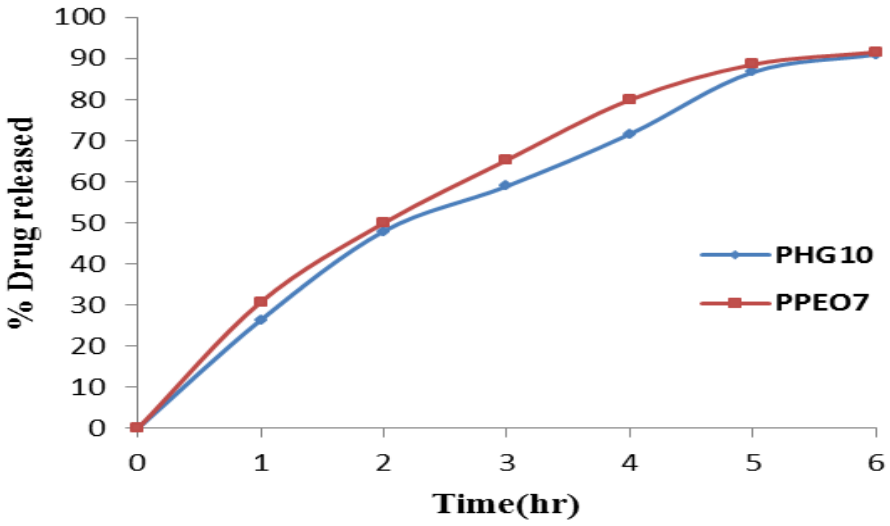


Figure 4: Release profile of mucoadhesive buccal patches of propranolol Hcl

CONCLUSION

Thus, the results of the present investigation concluded that the formaldehyde treated hupu gum used as mucoadhesive polymer in development of buccal patches of propranolol Hcl were prepared by solvent casting method. Hupu gum is highly viscous, difficult to form buccal patches, due to this reason it is exposed to formaldehyde for 1hr to reduce its swelling nature. However, the variation in the release profile of propranolol Hcl due to different in the drug to polymer ratio. Our results supported that formaldehyde exposed hupu gum is suitable

natural polysaccharide for development mucoadhesive buccal patches.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

ACKNOWLEDGEMENTS

Declared none.

PATIENT CONSENT

Declared none.

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